UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,356	06/03/2005	Klaus Dietzel	26794U	2653

34375 7590 11/20/2008

NATH & ASSOCIATES PLLC
112 South West Street
Alexandria, VA 22314

EXAMINER	
JEAN-LOUIS, SAMIRA JM	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
11/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,356	DIETZEL ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11 and 13-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This Office Action is in response to the remarks submitted on 08/12/08. Claims 6-11 and 13-17 are currently pending in the application, with claims 1-5, 12, and 18-24 having being cancelled. Accordingly, claims 6-11 and 13-17 are being examined on the merits herein.

Applicant's argument with respect to Postma et al. who does not teach a method of treating airway disease in a patient comprising administering a therapeutically effective amount of ciclesonide and R,R-formoterol wherein a ciclesonide and R,R-formoterol are present in separate pack units such that they are available for successive inhalative administration has been fully considered. Examiner would like to respectfully point out that the Postma reference was not used in the rejection filed on 05/13/08. Second, the arguments are moot since the rejection of claims 11-17 in view of Postma et al. was withdrawn due to applicant's amendment and cancellation of claim 12. Examiner simply rebutted applicant's arguments in the Response to arguments section filed on 05/13/08 as to why the Postma et al. reference rendered the claims obvious as originally presented. Thus, given that the rejection of claims 11-17 in view of Postma was withdrawn, applicant's arguments are now moot.

Applicant's contention that Magee in view of Calatayud et al. do not teach or suggest all of the elements of the presently pending claims have been fully considered but is not found persuasive. Magee clearly teaches the use of ciclesonide in conjunction with formoterol for the treatment of several diseases including bronchitis, COPD, and asthma which are all airway diseases. Magee further teaches that the composition can be formulated by nasal aerosol or inhalation forms. Importantly, Magee teaches that the compounds and therapeutic agents can be administered sequentially wherein each component is formulated apart from each other into separate dosage forms and ingested at consecutive times. Calatayud, on the other hand, was provided to demonstrate that the R-epimer of formoterol is highly effective in pharmacological activity and possess minimal systemic effects. Additionally, given that Magee teaches the use of its composition as a separate dosage units for ingestion at consecutive times, this necessarily reads on applicant's limitation of providing the composition in separate pack units such that they are available for successive inhalative administration. Further, the inclusion of a package insert or label showing "the name of drug, dosage form, route of administration, indication and direction of use" of a pharmaceutical composition is mandated by 21 CFR 201.57 and is therefore obvious to one of ordinary skill in the art. Thus, Magee in view of Calatayud et al. do indeed render obvious applicant's invention. Thus, the rejection of claims 6-11 and 13-17 over Magee in view of Calatayud et al. **is maintained**.

Applicant's argument with respect to Keller who teaches moisture resistant dry powder inhalation and inclusion of magnesium stearate rather than teach all of the presently pending claims has been fully considered but is not found persuasive. First, the Examiner would like to point out that the claims contain the claim language "comprising" which does not exclude addition of other components such as magnesium stearate. Moreover, Keller et al. was used to demonstrate why one of ordinary skill in the art would be motivated to use the formeterol salts of Keller since such formulations provided improved moisture resistance which necessarily affect the stability of the compounds. As previously discussed, Magee teaches the combination of ciclesonide and formoterol, and Calatayud et al. teach the R-epimer of ciclesonide with high anti-inflammatory properties. Thus, one of ordinary skill in the art would have found it obvious to substitute the formoterol of Keller into the composition of Magee and combined it with the R-epimer of ciclesonide as taught by Calatayud et al. with the reasonable expectation of obtaining a composition that is resistant to moisture and a composition effective in treating airway diseases. As for applicant's arguments that the aforementioned references do not teach separate pack units, such arguments are not persuasive as Magee teaches administration of the compounds sequentially (i.e. one after the other) at consecutive times. Moreover, one of ordinary skill in the art would have found it obvious to formulate the compounds in a unit pack given that such administration is well-known in the art. Thus, the Examiner contends that a *prima facie* case was indeed made and that Keller in view of Magee and in further view of

Calatayud render obvious applicant's invention. Consequently, the rejection of claims 6-11 and 13-17 in view of Keller **is also maintained**.

For the reasons, the rejections of claims 6-11 and 13-17 under 103 (a) remain proper and are maintained. However, for applicant's convenience the rejections are re-stated below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-11 and 13-17 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Magee et al. (2002/0111495 A1, previously submitted) in view of Calatayud et al. (U.S. 5,482,934, previously submitted).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor

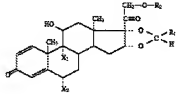
and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Magee et al. teach compounds of formula I useful as inhibitors of PDE4 in the treatment of diseases especially asthma, chronic bronchitis, and chronic obstructive pulmonary disease (abstract and pg. 1, paragraph 0006). Magee et al. further teach that the compounds may be made in a composition together with a pharmaceutical carrier for treating a number of diseases including bronchitis, obstructive bronchitis, COPD, allergic asthma and bronchial asthma (instant claim 15; see pg. 32, paragraphs 0190-0194). Magee et al. further teach the combination of a compound of formula I together with one or more therapeutic agents including formoterol and ciclesonide (see pg. 34, paragraph 0218, and pg. 98, paragraphs 0620, 0630, and 0636). These compounds and therapeutic agents are administered to a patient in combination with the compounds of formula I where they are sequentially administered where each component is formulated apart from each other into separate dosage forms and which are ingested at consecutive times by said patient with a significant time interval in between each ingestion (i.e. free combination administered successively; instant claims 6 and 11; see pg. 92 paragraphs 0571-0572). The compounds and therapeutic agents according to Magee et al. may be in the form of salts or acid salts including acetate, citrate, fumarate, gluconate, hydrochloride, hydrobromide, nitrate, sodium phosphate,

stearate, sulfate, sulfosalicylate and tartrate (instant claims 9-10; see pg. 99-100, paragraphs 0672, 0674 and 0676) and may be administered in various dosages and follow various treatment regimen depending upon a variety of factors including drug combination, age, body weight, general health, sex, diet, time of administration, rate of excretion, physician's judgment and severity of the disease (instant claims 11, 16-17; see pg. 99, paragraph 0671). Finally, Magee et al. teach that the pharmaceutical composition may be administered by nasal aerosol or inhalation through the use of a dry powder inhaler (instant claims 6, 11 and 14; see pg. 104, paragraphs 0709 and 0719).

Magee et al. do not specifically teach the R-epimer in an amount greater than 95% in the pharmaceutical composition.

Calatayud et al. teaches compounds of the general formula



with X1 an X2 corresponding to H and R1 is a phenyl group and R2 represents radicals such as C=OCH(CH3)CH3 in the form of an R epimer, S epimer or mixture of the R and S epimers (i.e. ciclesonide) as drugs and/or therapeutic agents (see abstract and col. 3, lines 1-61). Calatayud et al. further teach that these compounds possess intense pharmacological activity with no or minimal systemic effects (see col. 2 lines 21-23, col. 15, lines 10-11 and col. 16, lines 27-30). Calatayud et al. also teach synthesis of the

mixture of ciclesonide with both the R and S epimers which are then further purified to obtain either of the epimers in a proportion of at least 99.9% (see col. 11, lines 21-61 and col. 17-18, table II, compound 9). Importantly, Calatayud et al. teach that the R-epimer of ciclesonide possesses high anti-inflammatory activity, high glucocorticoid activity and high therapeutic index (see col. 17-18, table 3 compound 9).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the R-epimer into the composition of Magee et al. to treat airway diseases since Calatayud et al. teach that the R-epimer possesses intense glucocorticoid activity with minimal systemic effects. Given that Magee et al. teach a pharmaceutical composition comprising compounds of formula I together with ciclesonide and formoterol, and Calatayud et al. teach R-epimers of ciclesonide with high glucocorticoid activity, anti-inflammatory activity and minimal systemic effects, one of ordinary skill would have been motivated to incorporate the R-epimer of ciclesonide into the composition of Magee et al. with the reasonable expectation of providing a pharmaceutical composition that is efficacious in treating airway diseases and a composition that is readily absorbed with no systemic effects.

Claims 6-11 and 13-17 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Keller et al. (U.S. 6,645,466 B1, previously submitted) in view of Magee et al. (2002/0111495 A1, previously submitted) and in further view of Calatayud et al. (U.S. 5,482,934, previously submitted).

The Magee and Calatayud references are as discussed above and incorporated by reference herein.

Keller et al. teach dry powder formulations for inhalation (i.e. instant claim 6) containing a pharmaceutically effective carrier, pharmaceutically active compounds and magnesium stearate (see abstract and col. 4, lines 55-67). Keller et al. further teach that magnesium stearate is added to dry powder formulations which contain a beta mimetic in the form of salt such as formoterol fumarate or formoterol tartrate (instant claims 9-10), and/or an anticholinergic and/or a corticosteroid including ciclesonide (instant claim 6; see col. 6, lines 52-64 and col. 7, lines 5-10). The amount of active compounds in the formulations can vary within wide ranges or from 0.1-10% (instant claim 16).

Keller et al. do not specifically teach a composition comprising administering daily ciclesonide and formeterol from separate pack units for successive inhalation. Similarly, Keller et al. do not teach a method of treating airway diseases or the inclusion of the R-epimer of ciclesonide in the composition.

As previously stated, Magee et al. teach pharmaceutical composition for the treatment of airway diseases including asthma and COPD containing compounds of formula I along with ciclesonide and formoterol where they are sequentially administered, and where each component is formulated apart from each other into

separate dosage forms (i.e. separate pack unit) which are ingested at consecutive times (i.e. successive times) by a patient with a significant time interval in between each ingestion (i.e. free combination administered successively; instant claims 6, 11, and 15; see pg. 92 paragraphs 0571-0572). Moreover, Magee et al., also teach that these agents may be administered in various dosages and follow various treatment regimen depending upon a variety of factors (instant claims 11, 16-17; see pg. 99, paragraph 0671).

Calatayud et al. teach synthesis of the mixture of ciclesonide with both the R and S epimers and which are then further purified to obtain either of the epimers in a proportion of at least 99.9% (see col. 11, lines 21-61 and col. 17-18, table II, compound 9). Importantly, Calatayud et al. teach that the R-epimer of ciclesonide possesses high anti-inflammatory activity, high glucocorticoid activity and high therapeutic index (see col. 17-18, table 3 compound 9).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the R-epimer of Calatayud et al. into the composition of Keller et al. since Calatayud et al. teach that the R-epimer of ciclesonide possesses high anti-inflammatory activities. Likewise, it would have been obvious to one of ordinary skill in the art at the time of the invention to vary the treatment regimen as taught by Magee et al. and use the aforementioned composition for the treatment of airway diseases since Magee et al. teach the same type of composition for the treatment of asthma and COPD. Given that Keller teaches dry powder inhaler moisture-resistant compositions containing ciclesonide and formoterol or their salts, and

Magee et al. teach pharmaceutical composition containing compounds of formula I along with ciclesonide and formoterol for the treatment of airway diseases including asthma and COPD, and Calatayud et al. teaches R-epimers of ciclesonide with high glucocorticoid activity, anti-inflammatory activity and minimal systemic effects, one of ordinary skill would have been motivated to incorporate the R-epimer of ciclesonide into the composition of Keller et al. and used such composition for the treatment of airway diseases as taught by Magee et al. with the reasonable expectation of providing a pharmaceutical composition that is efficacious in treating asthma and COPD and a composition that produces no systemic effects.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1617

11/18/2008

/Shengjun Wang/

Primary Examiner, Art Unit 1617